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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,870	08/30/2005	Pei-Ran Wang	PC/4-32778A	6797

1095 7590 06/04/2007

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
HUGHES, ALICIA R	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
06/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,870	WANG, PEI-RAN	
	Examiner	Art Unit	
	Alicia R. Hughes	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *09 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-28* is/are pending in the application.

4a) Of the above claim(s) *29-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 page*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 21-31 are pending and the subject of this Office Action. Claims 21-28 are presented, however, for examination. Applicant's election of species, without traverse, in the reply filed on 9 February 2007 is acknowledged. Claims 29-31 are withdrawn from consideration, as they are part of a non-elected invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 21-28 (composition claims) and claims 29-31 (method claims) are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 (composition claims) and 11-16 (method claims) of U.S. Patent Application No. 11/571,994. Although the conflicting claims are not identical, they are not patentably distinct from each other. Just as with claims 21-28 of the instant invention, claims 1-10 of Application '994 are drawn to a composition comprising a PPARα agonist in combination with GLP-1 agonists. It is known in the art that DPP-IV inhibitors are GLP-1 analogues. *See* U.S. Patent Application No. 2002/0065239, page 6, para. 77, lines 1-5.

Claims 29-31 of the instant application and 11-16 in Application '994 merely recite the methods which encompass the composition claims for the treatment in the instant case of dyslipidemia, obesity, diabetes mellitus, osteoporosis, and arthritis, etc. Similarly, claims 11-16 of the '995 Application teaches the same composition as useful in a method to treat diabetes, hyperlipidemic disease, metabolic diseases and disorders, and addictions. As a result, the variations would have been obvious to the skilled artisan at the time the first invention was contemplated to use these pharmaceuticals to treat diabetes mellitus and related conditions. This

is a provisional obviousness-type double patenting rejection, since the claims have not, in fact, been patented.

Claim Rejections – 35 U.S.C. §102(e)

The following is a quotation of 35 U.S.C. §102(e), which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> ...
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

For the purpose of examination herein, the pending claims are given their broadest reasonable interpretation in light of the supporting disclosure. *In re Morris*, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997). Limitations appearing in the specification but not recited in the claim should not be read into the claim. *E-Pass Techs., Inc. v. 3Com Corp.*, 343 F.3d 1364, 1369, 67 USPQ2d 1947, 1950 (Fed. Cir. 2003) (claims must be interpreted "in view

of the specification" without importing limitations from the specification into the claims unnecessarily). *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969).

Claims 21-26 are rejected under 35 U.S.C. §102(a) or §102(e) as being anticipated by U.S. Patent Publication No. 2002/0065239 [hereinafter referred to as "Caplan et al"].

Caplan et al teach compositions for the treatment of diabetes, obesity and diabetic-related conditions by the administration of a therapeutically effective amount of "vectors encoding the following: glucokinase regulatory protein alone or co-administered with glucokinase or with metabolism modifying proteins; glucokinase co-administered with metabolism modifying proteins; or glucokinase regulatory protein co-administered with glucokinase in combination with metabolism modifying proteins" ... and "[a]dditionally, PPARα ligands and DPP-IV inhibitors may be co-administered with the above (Abstract; see also Page 2, paras. 13 and 14).

Caplan et al also teach that "[r]epresentative PPARα ligands which are employed in the present invention include, but are not limited to fibrates, for example, clofibrate, fenofibrate, bezafibrate, ciprofibrate, beclofibrate, etofibrate and gemfibrate" (Page 6, para. 0071, lines 1-5), and that "[c]o-expression of GK alone or GK and GKRP wit GLP-1 or an inhibitor of the enzyme that inactivates GLP-1, i.e. an inhibitor of dipeptidyl peptidase IV (DPP-IV), may be employed to treat diabetes and obesity" (Page 6, para. 77, lines 1-5). Caplan et al teach that "[p]referred examples of DPP-IV inhibitors include *N*-(N'-substituted glycyl)-2-cyanopyrrolidines ..." (Page 7, para. 80), as disclosed in U.S. Patent No. 6,011,155 [hereinafter referred to as "Villhauer et al"].

Caplan et al also note the several modes of administration dosage ranges and periods and notes that "[I]t is noted that the clinician or treating physician will know how and when to adjust,

interrupt or terminate therapy in conjunction with individual patient response (Page 9, para. 102). More specifically, Caplan et al note "The PPARα ligands and DPP-IV inhibitors are administered using convenient administration techniques including intravenous, intradermal, intramuscular, subcutaneous, oral. Oral dosing is preferred. For oral dosing, the compounds are combined with pharmaceutically acceptable carriers and formulated into tablets or capsules and the like (Page 9, para. 102). It is well understood in the art that solid fixed combination forms and combination preparations can be capsules or tablets. See U.S. Patent No. 6,086,919, Col. 4, lines 50-52; Col. 14, lines 28-39; Col. 15, lines 8-12; see also U.S. Patent No. 6,559,188, Col. 6, lines 35-41 and 66-67 through Col. 7, line 1.

In light of the foregoing, a composition comprising a DPP-IV inhibitor that is a *N*-(N'-substituted glycyl)-2-cyanopyrrolidine in combination with a PPARα receptor, is clearly anticipated.

Claim Rejections – 35 U.S.C. §103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

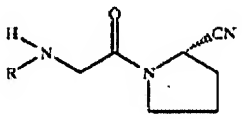
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 27 and 28 are rejected as being unpatentable over Caplan et al in view of Villhauer. The teachings of Caplan et al, *supra*, are incorporated herein by reference, in total. Caplan et al do not teach the specifc DPP-IV inhibitors disclosed in claims 27 and 28 of the referenced invention. However, Villhauer teaches

N-(N'-substituted glycyl)-2-cyanopyrrolidines of formula I



I

Compounds of formula I inhibit DPP-IV (dipeptidyl-peptidase-IV) activity. They are therefore indicated for use as pharmaceuticals in inhibiting DPP-IV and in the treatment of conditions mediated by DPP-IV, such as non-insulin-dependent diabetes mellitus, arthritis, obesity, osteoporosis and further conditions of impaired glucose tolerance.

(Abstract).

Villhauer teaches, more specifically, a pharmaceutical composition comprising the compound "in free form or in a pharmaceutically acceptable acid addition salt form, together with at least one pharmaceutically acceptable carrier or diluent" (Col. 38, lines 18-22, claim 10) and that the DPP-IV inhibitor may be, for example, 1-[2-[(5cyanopyridin-2-yl)amino] ethylamino]acetyl-2-cyano-(S)-pyrrolidine, in free form or in acid addition salt form (Col. 35, lines 18-22, claim 8) or Pyrrolidine, 1-[(1-adamantyl)amino]acetyl-2-cyano-,(S)-monohydrochloride (Col. 37, lines 3-4) or a pharmaceutically acceptable salt of such compounds

which are in free form (Col 38, lines 16-17) as the DPP-IV inhibitor that can be utilized for these types of various diseases, including diabetes mellitus.

While Villhauer does not explicitly disclose (S)-1-[(3-hydroxy-1-adamantyl)amino]acetyl-2-cyano-pyrrolidine, it does for example, disclose Pyrrolidine, 1-[(1-adamantyl)amino]acetyl-2-cyano-,(S)-monohydrochloride, of which the elected compound is an obvious variant.

One of ordinary skill in the art would be motivated to combine the teachings of Caplan et al with the teachings of Villhauer, because the references teach overlapping subject matter, treatment of diabetes and related conditions utilizing DPP-IV inhibitors and Caplan refers to Villhauer as teaching DPP-IV inhibitors part of the preferred embodiment of their invention.

In light of the foregoing, it would have been *prima facie* obvious to one of ordinary skill in the art to combine DPP-IV inhibitors such as, for example, (S)-1-[(3-hydroxy-1-adamantyl)amino]acetyl-2-cyano-pyrrolidine, in free form or in acid addition salt form with PPARα ligands such as micronized fenofibrate, thereby, rendering the present invention obvious.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alicia Hughes whose telephone number is 571-272-6026. The examiner can normally be reached from 9:00 AM to 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR of Public PAIR. Status information for unpublished applications is available through Public PAIR only. For information about the PAIR system, see http://pair-direct-uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

28 May 2007
ARH

BRIAN-YONG S. KWON
PRIMARY EXAMINER